IN THE CLAIMS

Amend the claims as indicated below by the markings. Cancel claims 31 and 32 without prejudice.

1. (Previously Presented) A transgenic mutant mouse deficient in an endogenous Sigma-1 receptor, whose genome comprises a mutation comprising a disruption in a gene of an endogenous Sigma-1 receptor, wherein said gene disruption gives rise to a transgenic mutant mouse lacking detectable levels of endogenous Sigma-1 receptor, and wherein said transgenic mutant mouse is fertile and obtainable by the use of the vector identified as pHR53TK that is deposited in the CECT under access number CECT 5737, to insert a functional disruption in the endogenous Sigma-1 receptor.

2. (Previously Presented) The transgenic mutant mouse according to claim 1, wherein said transgenic mutant mouse is a heterozygous mutant for said mutation.

3. (Previously Presented) The transgenic mutant mouse according to claim 1, wherein said transgenic mutant mouse is a homozygous mutant for said mutation.

Claim 4. (Cancelled)

5. (Previously Presented) The transgenic mutant mouse according to claim 1, wherein the genome of the transgenic mutant mouse comprises a transgene within the disrupted region introduced in the endogenous Sigma-1 receptor gene that comprises a sequence encoding a positive selection marker.

6. (Previously Presented) The transgenic mutant mouse according to claim 5, wherein said transgene comprises the neomycin phototransferase (*neo*) gene.

Claim 7. (Cancelled)

8. (Previously Presented) The transgenic mutant mouse according to claim 1, wherein said transgenic mutant mouse is deficient in the endogenous Sigma-1 receptor, homozygous

for the mouse Sigma-1 receptor gene, and fertile, whose genome contains a disruption in said transgene comprising the *neo* gene.

9. (Previously Presented) A homologous recombination vector with positive-negative selection, comprising:

a first homology region positioned at the 5' end of a nucleotide sequence encoding a positive selection marker, wherein said first homology region has a nucleotide sequence that is substantially identical to a first sequence of a Sigma-1 receptor gene;

a nucleotide sequence encoding a positive selection marker;

a second homology region positioned at the 3' end of said nucleotide sequence encoding a positive selection marker, wherein said second homology region has a nucleotide sequence that is substantially identical to a second nucleotide sequence of said Sigma-1 receptor gene, this second sequence of the Sigma-1 receptor gene being positioned at 3' to the first sequence of the Sigma-1 receptor gene in a wild type endogenous Sigma-1 gene;

a nucleotide sequence encoding a negative selection marker;

identified as pHR53TK, deposited in Spanish Type Culture Collection (CECT) of the University of Valencia with access number CECT 5737.

Claims 10 – 13. (Canceled)

14. (Previously Presented) An isolated non-human mammal host cell whose genome comprises an endogenous Sigma-1 receptor gene transfected with a homologous recombination vector with positive-negative selection according to claim 9, deficient in an endogenous Sigma-1 receptor.

15. (Previously Presented) The cell according to claim 14, wherein said isolated non-human mammal host cell whose genome contains an endogenous Sigma-1 receptor gene is selected from the group consisting of a differentiated cell that normally expresses the product of the Sigma-1 receptor gene and a pluripotent embryonic cell.

16. (Previously Presented) The isolated non-human mammal host cell according to claim 14, comprising an allele of the mutated Sigma-1 receptor gene.

17. (Previously Presented) An isolated cell from a transgenic mouse, deficient in an endogenous Sigma-1 receptor, according to claim 1, or its offspring.

18. (Previously presented) The cell according to claim 17, comprising one or both mutated alleles of the Sigma-1 receptor gene.

19. (Previously presented) The cell according to claim 17, wherein the cell is propagated.

20. (Previously Presented) The offspring of a transgenic mutant mouse deficient in an endogenous Sigma-1 receptor, according to claim 1.

21. (Previously presented) A process for making a mutant mouse according to claim 1, comprising:

introducing a functional disruption in an endogenous Sigma-1 receptor gene present in a cell genome by homologous recombination in said cell between an allele of an endogenous Sigma-1 receptor gene and a homologous recombination vector with positive-negative selection according to claim 9,

selecting the recombinant homologues by the positive-negative selection technique,

introducing said recombinant homologues in embryos,

implanting said embryos receptor pseudogestating female mammals,

carrying, by the female mammals, the embryos to term,

selecting chimeras able to efficiently transmit the genotype of the recombinant homologues to their offspring by the germ line, and

crossing said chimeras with wild-type mice to obtain heterozygous mutants to disrupt the endogenous Sigma-1 receptor.

Claims 22 – 27. (Canceled)

28. (Previously presented) The cell according to claim 19 wherein the cell is immortalized.

29. (Previously presented) The process according to claim 21, further comprising: crossing said heterozygous mutants with each other to obtain homozygous mutants.

Claims 30, 31 and 32. (Cancelled)